

Application Serial No. 10/759,841

-2-

Docket No. 023004.0104N3US

Amendments To The ClaimsRECEIVED
CENTRAL FAX CENTER
OCT 31 2006

1-65. (Cancelled)

66. (Currently Amended) ~~An isolated~~ synthetic genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct,

wherein said genetic construct comprises ~~at least~~ two copies of a structural gene sequence connected in a head-to-head, head-to-tail or tail-to-tail orientation relative to each other, operably linked to and at least one a terminator sequence which contains a polyadenylation signal and is active in the cell,

wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to ~~at least~~ a region of said target gene,

wherein said ~~at least~~ two copies of said structural gene sequence are placed operably under the control of a single promoter sequence which is operable in said cell, where in at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of said promoter sequence, wherein said two copies of said structural gene sequence are separated by a stuffer fragment which comprises a sequence of nucleotides;

and wherein said ~~at least one said~~ terminator sequence is operably linked to ~~at least one a~~ said two copies ~~copy~~ of said structural gene sequence.

3667620

BEST AVAILABLE COPY

Application Serial No. 10/759,841

-3-

Docket No. 023004.0104N3US

67. (Currently Amended) ~~An isolated~~ synthetic genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said genetic construct,

wherein said genetic construct comprises ~~at least~~ two copies of a structural gene sequence connected in a head-to-head, head-to-tail or tail-to-tail orientation relative to each other, and at least two terminator sequences each of which contains a polyadenylation signal and is active in the cell,

wherein each copy of said structural gene sequence is separately placed under the control of a promoter which is operable in said cell and one of said terminator sequences, and

wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to ~~at least~~ a region of said target gene,

wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence;

and wherein said two copies of said structural gene sequence are separated by a stuffer fragment which comprises a sequence of nucleotides;

and

~~wherein at least one each of said terminator sequence is operably linked to at least one copy of said structural gene sequence.~~

68. (Presently Presented) The isolated genetic construct of claim 66,

wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of said promoter sequence.

3667620

Application Serial No. 10/759,841

-4-

Docket No. 023004.0104N3US

69. (Presently Presented) The isolated genetic construct of claim 67, wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of another individual promoter sequence.

70. (Cancelled).

71. (Cancelled).

72. (Currently Amended) The isolated genetic construct according to claim 66, ~~comprising~~ having only two copies of said structural gene sequence.

73. (Currently Amended) The isolated genetic construct according to claim ~~68~~6, wherein said region of the target gene is ~~at least about~~ 30 nucleotides long.

74. (Currently Amended) The isolated genetic construct according to claim ~~68~~6, wherein said structural gene sequence comprises a nucleotide sequence that is identical to said region of said target gene.

75. (Currently Amended) A method of delaying or repressing the expression of a target gene in an animal cell, comprising transfecting said animal cell with the genetic construct of claim 66.

3667620

Application Serial No. 10/759,841

-5-

Docket No. 023004.0104N3US

76. (Presently Presented) The method according to claim 75, wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of said promoter sequence.

77. (Cancelled).

78. (Cancelled).

79. (Currently Amended) The method according to claim ~~76~~5, wherein said genetic construct ~~comprises~~ has only two copies of said structural gene sequence.

80. (Currently Amended) The method according to claim ~~76~~5, wherein said region of the target gene is ~~at least about~~ 30 nucleotides long.

81. (Cancelled).

82. (Presently Presented) An animal cell comprising the genetic construct according to claim 66.

83-114 (Cancelled)

115. (New) The genetic construct of claim 68, wherein the target gene is a viral gene

3667620

Application Serial No. 10/759,841

-6-

Docket No. 023004.0104N3US

116. (New) The genetic construct of claim 115, wherein the viral gene encodes a DNA polymerase, RNA polymerase or viral coat protein.

117. (New) The genetic construct of claim 68, wherein the target gene is from a lentivirus.

118. (New) The genetic construct of claim 68, wherein the target gene is from an immuno deficiency virus.

119. (New) The genetic construct of claim 68, wherein the target gene is from a single-stranded (+) RNA virus.

120. (New) The genetic construct of claim 68, wherein the target gene is from a double-stranded DNA virus.

121. (New) The genetic construct of claim 68, wherein the target gene is a transgene in the animal cell.

122. (New) The genetic construct of claim 68, wherein the target gene is an endogenous gene of the animal cell.

123. (New) The genetic construct of claim 68, wherein the region of the target gene corresponds to a coding region of the target gene.

3667620

Application Serial No. 10/759,841

-7-

Docket No. 023004.0104N3US

124. (New) The genetic construct of claim 68, wherein the region of the target gene corresponds to a 5'- or 3'- untranslated sequence of the target gene.

125. (New) The genetic construct of claim 68, wherein the transcribed region of the genetic construct comprises an intron.

126. (New) The genetic construct of claim 68, wherein the stuffer fragment is a sequence of nucleotides 10-50 nucleotides in length, 50-100 nucleotides in length, or 100-500 nucleotides in length.

127. (New) The genetic construct of claim 68, wherein the stuffer fragment comprises an intron.

128. (New) The genetic construct of claim 68, wherein the total length of said structural gene sequences is no more than 2.0 kilobases.

129. (New) The genetic construct of claim 128, wherein the total length of said structural gene sequences is no more than 0.5 kilobases.

130. (New) The genetic construct of claim 68, wherein the two copies are in a head-to-head orientation relative to each other.

3667620

Application Serial No. 10/759,841

-8-

Docket No. 023004.0104N3US

131. (New) The genetic construct of claim 68, wherein the two copies are in a tail-to-tail orientation relative to each other.

132. (New) The genetic construct of claim 68, wherein the two copies are identical in sequence.

133. (New) The genetic construct of claim 68, wherein the two copies are not identical in sequence.

134. (New) The genetic construct of claim 68, which is in a cell.

135. (New) The genetic construct of claim 68, which is in a virus particle.

136. (New) The genetic construct of claim 68, which is in a liposome.

137. (New) The genetic construct of claim 134, which is integrated into the genome of the cell.

138. (New) An animal cell, comprising the genetic construct of claim 68.

139. (New) The animal cell of claim 138, wherein the target gene is a viral gene.

3667620

Application Serial No. 10/759,841

-9-

Docket No. 023004.0104N3US

140. (New) The animal cell of claim 139, wherein the viral gene encodes a DNA polymerase, RNA polymerase or viral coat protein

141. (New) The animal cell of claim 138, wherein the target gene is from a lentivirus.

142. (New) The animal cell of claim 138, wherein the target gene is from an immunodeficiency virus.

143. (New) The animal cell of claim 138, wherein the target gene is from a single-stranded (+) RNA virus.

144. (New) The animal cell of claim 138, wherein the target gene is from a double-stranded DNA virus.

145. (New) The animal cell of claim 138, wherein the target gene is a transgene in the animal cell.

146. (New) The animal cell of claim 138, wherein the target gene is an endogenous gene of the animal cell.

147. (New) The animal cell of claim 138, wherein the region of the target gene corresponds to a coding region of the target gene.

3667620

Application Serial No. 10/759,841

-10-

Docket No. 023004.0104N3US

148. (New) The animal cell of claim 138, wherein the region of the target gene corresponds to a 5'- or 3'- untranslated sequence of the target gene.

149. (New) The animal cell of claim 138, wherein the transcribed region of the genetic construct comprises an intron.

150. (New) The animal cell of claim 138, wherein the stuffer fragment is a sequence of nucleotides 10-50 nucleotides in length, 50-100 nucleotides in length, or 100-500 nucleotides in length.

151. (New) The animal cell of claim 138, wherein the stuffer fragment comprises an intron.

152. (New) The animal cell of claim 138, wherein the total length of said structural gene sequences is no more than 2.0 kilobases.

153. (New) The animal cell of claim 152, wherein the total length of said structural gene sequences is no more than 0.5 kilobases.

154. (New) The animal cell of claim 138, wherein the two copies are in a head-to-head orientation relative to each other.

3667620

Application Serial No. 10/759,841

-11-

Docket No. 023004.0104N3US

155. (New) The animal cell of claim 138, wherein the two copies are in a tail-to-tail orientation relative to each other.

156. (New) The animal cell of claim 138, wherein the two copies are identical in sequence.

157. (New) The animal cell of claim 138, wherein the two copies are not identical in sequence.

158. (New) The animal cell of claim 138, which is integrated into the genome of the cell.

159. (New) The animal cell of claim 138, wherein the promoter is heterologous with respect to the structural gene sequence.

160. (New) The animal cell of claim 138, wherein the promoter is expressed before the commencement of detectable expression of the target gene in the cell.

161. (New) The animal cell of claim 138, wherein the gene construct is expressed to produce a primary transcript which has a polyadenylate sequence added to the 3'-end.

162. (New) An isolated animal cell, tissue or organ, comprising the genetic construct of claim 68.

3667620